LISTING OF THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in this application.

1-55. (canceled)

56. (currently amended) A method of preparing a multispecific antibody comprising at least four polypeptides, ~~first polypeptide and at least one additional polypeptide,~~ the method comprising the steps of:

(i) culturing a host cell comprising nucleic acids encoding the polypeptides, such that the polypeptides are expressed and form a multispecific antibody; ~~a nucleic acid encoding a first polypeptide and a nucleic acid encoding at least one additional polypeptide, so that the nucleic acids are expressed;~~ wherein

(a) a ~~the~~ first polypeptide and a second polypeptide ~~each at least one additional polypeptide~~ each comprise a multimerization domain and a heavy chain constant domain, and the multimerization domain of the first polypeptide interacts with the multimerization domain of the second polypeptide; and ~~comprising a multimerization domain, and the multimerization domain of the first polypeptide forms an interface positioned to interact with an interface of the multimerization domain of the at least one additional polypeptide;~~

(b) a third polypeptide and a fourth polypeptide each comprise a light chain variable domain having ~~the first polypeptide and each at least one additional polypeptide each further comprise a binding domain comprising a heavy chain variable domain and a light chain variable domain, wherein each binding domain binds to a different antigen and each light chain variable domain has~~ the same amino acid sequence, and each light chain variable domain together with one of the heavy chain variable domains, forms a binding domain that binds to a different antigen; and

(c) ~~the multimerization domain of the first polypeptide interacts with the multimerization domain of the at least one additional polypeptide to form a multispecific antibody; and;~~

(ii) recovering the multispecific antibody from the host cell culture.

57. (currently amended) The method of claim 56, wherein the multimerization domain of either the first polypeptide or the second ~~at least one additional~~ polypeptide, or of both the first polypeptide and the second polypeptide, is altered by amino-acid substitution to form a non-naturally occurring disulfide bond between a free thiol-containing residue in the multimerization domain of the first polypeptide and ~~a free thiol-containing residue in the multimerization domain of the first polypeptide and~~ a free thiol-containing residue in the multimerization domain of the second ~~at least one additional~~ polypeptide.

58. (currently amended) The method of claim 56, wherein the interaction between the multimerization domain of the first polypeptide and the second ~~at least one additional~~ polypeptide comprises a protuberance-into-cavity interaction.

59. (currently amended) The method of claim 58, wherein the protuberance is generated by altering the first polypeptide by substituting an amino acid of the first polypeptide with an amino acid that has a larger side chain volume than the substituted amino acid, and the cavity is generated by altering the second ~~at least one additional~~ polypeptide by substituting an amino acid of the second ~~at least one additional~~ polypeptide with an amino acid that has a smaller side chain volume than the substituted amino acid.

60. (previously presented) The method of claim 59, wherein the step of generating a protuberance or generating a cavity, or both, occurs by phage display selection.

61. (previously presented) The method of claim 59, wherein the amino acid residue having a larger side chain volume than the substituted amino acid is selected from the group consisting of arginine (R), phenylalanine (F), tyrosine (Y), tryptophan (W), isoleucine (I) and leucine (L).

62. (previously presented) The method of claim 59, wherein the amino acid residue having a smaller side chain volume than the substituted amino acid is selected from the group consisting of glycine (G), alanine (A), serine (S), threonine (T), and valine (V), and wherein the import residue is not cysteine (C).

63. (previously presented) The method of claim 56, wherein the heavy chain constant domain is selected from the group consisting of a C_H3 domain and a heavy chain constant domain of an IgG.

64. (currently amended) The method of claim 56 wherein step (i) is preceded by a step of introducing the nucleic acids ~~encoding the first polypeptide and the at least one additional polypeptide~~ into the host cell.

65. (previously presented) An isolated host cell comprising the nucleic acids encoding the multispecific antibody of claim 56.

66. (previously presented) The host cell of claim 65 wherein the host cell is a mammalian cell.

67. (currently amended) A method of preparing a multispecific antibody comprising at least four polypeptides, the method comprising the steps of:

(i) selecting nucleic acids encoding the polypeptides; ~~a nucleic acid encoding a first polypeptide, a nucleic acid encoding a light chain, and at least one additional nucleic acid encoding at least one additional polypeptide;~~

(ii) introducing into a host cell the nucleic acids; ~~encoding the first polypeptide, the nucleic acid encoding a light chain, and the at least one additional nucleic acid encoding at least one additional polypeptide;~~

(iii) culturing the cell so that the nucleic acids are expressed and form a multispecific antibody, wherein ~~encoding the first polypeptide, the nucleic acid encoding the light chain, and the at least one additional nucleic acid encoding the at least one additional polypeptide are expressed, wherein~~

(a) a ~~the~~ first polypeptide and a second polypeptide ~~each at least one additional polypeptide~~ each comprise a multimerization domain and a heavy chain constant domain, and the multimerization domain of the first polypeptide interacts with the multimerization domain of the second polypeptide; and ~~comprising a multimerization domain, and the multimerization domain of the first polypeptide forms an interface positioned to interact with an interface of the multimerization domain of the at least one additional polypeptide;~~

(b) a third polypeptide and a fourth polypeptide each comprise a light chain variable domain having ~~the first polypeptide and each at least one additional polypeptide each further comprise a binding domain comprising a heavy chain variable domain and a light chain variable domain, wherein each binding domain binds to a different antigen and each light chain variable domain has~~ the same amino acid sequence, and each light chain variable domain together with one of the heavy chain variable domains, forms a binding domain that binds to a different antigen; and

~~(c) the multimerization domain of the first polypeptide interacts with the multimerization domain of the at least one additional polypeptide to form a multispecific antibody; and;~~

(iv) recovering the multispecific antibody the cell culture.

68. (currently amended) The method of claim 67, wherein the interaction between the multimerization domain of the first polypeptide and the second ~~at least one additional~~ polypeptide comprises a protuberance-into-cavity interaction.

69. (currently amended) The method of claim 67, wherein the multimerization domains of the first polypeptide and the second ~~at least one additional~~ polypeptide are altered to import a free thiol-containing residue into the first polypeptide and the second ~~at least one additional~~ polypeptide, such that the free thiol-containing residues interact to form a disulfide bond between the first polypeptide and the second ~~at least one additional~~ polypeptide.

70. (currently amended) The method of claim 67 wherein the first polypeptide and the second ~~at least one additional~~ polypeptide each comprise an antibody constant domain.

71. (previously presented) The method of claim 67 wherein the heavy chain constant domain is a C_H3 domain.

72. (previously presented) The method of claim 67 wherein the heavy chain constant domain is the constant domain of a human IgG.

73. (currently amended) A method of preparing a multispecific antibody comprising at least four polypeptides, ~~a first polypeptide and at least one additional polypeptide,~~ the method comprising the steps of:

(i) culturing a host cell comprising nucleic acids encoding the polypeptides; wherein ~~a nucleic acid encoding a first polypeptide and a nucleic acid encoding at least one additional polypeptide, so that the nucleic acids are expressed; wherein~~

(a) a ~~the~~ first polypeptide and a second polypeptide ~~each at least one additional polypeptide~~ each comprise a multimerization domain and a heavy chain constant domain, and the multimerization domain of the first polypeptide interacts with the multimerization domain of the second polypeptide; and ~~comprising a multimerization domain, and the multimerization domain of the first polypeptide forms an interface positioned to interact with an interface of the multimerization domain of the at least one additional polypeptide;~~

(b) a third polypeptide and a fourth polypeptide each comprise a light chain variable domain that have ~~the first polypeptide and the at least one additional polypeptide each further comprise a binding domain, the binding domain comprising a heavy chain and a light chain, wherein the common light chain of the first polypeptide and the at least one additional polypeptide has~~ at least 98% sequence identity and/or that only differ from each other ~~to a light chain of a first antibody and/or at least one additional antibody and only differs from each of the light chains of the first and/or at least one additional antibody~~ at amino acid positions outside of the CDR regions, and each light chain variable domain together with one of the heavy chain variable domains, forms a binding domain that binds to a different antigen; and ~~wherein the first and the at least one additional antibody bind to different antigens, and wherein each binding domain of the multispecific antibody binds to the different antigens; and~~

(ii) recovering the multispecific antibody from the host cell culture.

74. (canceled) ~~The method of claim 73, wherein the common light chain has 100% sequence identity to the light chain of the first antibody and the at least one additional antibody.~~

75. (currently amended) The method of claim 73, wherein each of the multimerization domains of the first polypeptide and the second ~~at least one additional~~ polypeptide comprise a C_H3 domain of an antibody constant domain.

76. (currently amended) The method of claim 75, wherein the multimerization domain of the first polypeptide has a protuberance and the multimerization domain of the second ~~at least one additional~~ polypeptide has a cavity, wherein the protuberance and the cavity interact to form a protuberance-into-cavity interaction.

77. (previously presented) The method of claim 76, wherein the multimerization domains further comprise a non-naturally occurring disulfide bond.